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# MONOCLONAL ANTIBODY IMPROVES SEPSIS

**TORONTO**--Treatment with the monoclonal antibody afelimomab increases survival in patients with severe sepsis or septic shock. It also speeds the reversal of organ failure in these patients, and the drug's safety profile is similar to that of placebo, according to findings of the MONARCS (Monoclonal Anti-TNF, A Randomized Controlled Sepsis) trial.[1] Preliminary results from this multicenter phase III clinical study of afelimomab in 2,634 patients with severe sepsis or septic shock were presented by Edward A. Panacek, MD, MPH, at the annual meeting of the American Thoracic Society.

## UNIQUE SEPSIS TREATMENT

Afelimomab, the F(ab´)2 fragment of a murine anti-tumor necrosis factor-alpha antibody, is the only molecule of its kind to undergo study as a treatment for sepsis, said Dr. Panacek, Professor of Medicine at the University of California Davis Medical Center in Sacramento. In phase II clinical trials, he noted, afelimomab had a dose-response effect on mortality in patients with sepsis--but only in those with baseline blood interleukin (IL)-6

levels above 1,000 pg/mL.[2]

To be eligible for the phase III trial, subjects had to have clinical signs of sepsis and "explicit, defined evidence of infection," explained Dr. Panacek. Patients were prospectively stratified into one of two groups according to their baseline IL-6 level. Next, they were randomized to either afelimomab or placebo, three times daily for three days. Afelimomab was administered at 1 mg/kg, the dose found to be most efficacious in the phase II trials.

About 40% of the study population had high baseline IL-6 levels, and this group was the primary focus of the analysis presented by Dr. Panacek. Both the afelimomab and placebo subgroups had similar baseline characteristics. Baseline sepsis severity (as measured by APACHE II and severity-of-illness scores) was also comparable. However, the patients given afelimomab had a higher mean Sepsis-related Organ Failure Assessment (SOFA) score.

Among the patients with high IL-6 levels, unadjusted all-cause mortality at 28 days was 43.65% for afelimomab recipients versus 47.65% for those given placebo--a 4% crude difference. This difference was statistically significant, however, and rose to 6.9% following adjustment for SOFA scores. The odds ratio for 28-day survival in the afelimomab group (compared with the placebo group) was 1.32.

"Recovery from organ dysfunction was faster in the group that received the monoclonal antibody," said Dr. Panacek. Multiple organ dysfunction syndrome scores also showed progressively greater improvement in the afelimomab group on days 3, 4, and 7 than in the placebo group.

The IL-6 level dropped more quickly in the afelimomab recipients, according to Dr. Paneck. The difference in IL-6 levels was apparent within eight hours after the start of afelimomab or placebo administration and remained significant at 72 hours.

Afelimomab appeared safe. The overall rate of adverse events and the incidence of secondary infection were similar in both groups, reported Dr. Panacek.

**--Timothy Begany**

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